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CHANGES IN APPETITE FOR WATER, GLUCOSE, SODIUM, AND POTASSIUM IN RATS WHEN THE SODIUM PUMP IS INHIBITED BY STROPHANTHIN-K

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ABSTRACT

It is found that strophanthin inhibits sodium appetite and stimulates potassium and water appetites. With strophanthin administration there is increased water appetite, decreased glucose consumption, decreased sodium consumption, and increased potassium consumption.

Existing theories on the regulation of water and salt appetite /1211* relate the elevated consumption of water and salts to a lack of the corresponding substances in the internal medium of the body. It has been shown, in particular, that reduction of blood sodium results in increased consumption of common salt; in cases of hypernatremia, decreased salt appetite is accordingly detected, and the thirst center is ordinarily greatly excited.

Holms and Gregerson (Ref. 6) have, however, already discovered that no correlation exists between the sodium content in the blood and water appetite. Subsequently, the lack of an inverse correlation was demonstrated by M. V. Arkind with respect to the salt appetite. The question has naturally arisen of whether the regulation of water and salt appetite may not depend, at least in some cases, not on the decrease or increase of the salt and water content in

*Note: Numbers in the margin indicate pagination in the original foreign text.

the internal environment of the body, but on mechanisms controlling the distribution of salts between the cell and the surrounding environment.

In verifying this hypothesis, it is expedient first of all to examine the relationship of the sodium pump to the regulation of water and salt appetite. This mechanism is known to be responsible for the non-equilibrium distribution of sodium and potassium between intra- and extracellular fluids.

Inhibition of the sodium pump leads to penetration of sodium into the cells and loss of potassium to the surrounding medium (Refs. 2-5, 11, 12, etc.).

This effect may be achieved in various ways. Of especial interest is the action of strophethin and its derivatives which specifically inhibit the sodium pump (Refs 7, 9, 10, 14).

The present work has studied the effect of strophanthin-K on rats' consumption of aqueous and saline glucose solutions under conditions of free choice. There is no change in the total reserves of mineral substances in the organism, and a change in alimentary reactions can depend only on their redistribution between extra- and intracellular fluids.

Methods. Experiments were conducted on white female rats of the Wistar line, 180-200 g in weight. The animals were placed in chambers with two automatic drinking bowls, each of which - depending on the purposes of the experiment - was filled with appropriate solutions. The drinking bowls were moved into the chambers for 10 sec. at 1 min. intervals, sixteen times during a single experiment. Level of appetite and choice were estimated from the number of approaches the animals made and the amount of the respective solutions which they drank.

The rats were offered a choice in the Ist series of experiments between a

40% solution of glucose in distilled water and a 40% solution of glucose in a 0.85% solution of sodium chloride. In the IInd series, the choice was between 8 and 40% solutions of glucose in distilled water. In the IIIrd series, the choices were (a) between a 40% solution of glucose in distilled water and a /1212
40% solution of glucose in a potassium chloride solution (the potassium was used in a concentration four times greater than in Ringer's solution), and (b) between an 8% solution of glucose in distilled water and an 8% solution of glucose in potassium chloride of the above-mentioned concentration. The total amount of glucose consumed characterized the alimentary appetite; the total amount consumed of the sodium chloride solution characterized the sodium appetite, etc.

A good linear dependence was noted between the number of approaches and the quantity of ingested solutions. Beforehand, a rather constant choice of solutions had been determined in the rats.

Strophanthin-K was intravenously administered in the amount of 0.3 - 0.15 ml of 0.05% solution 30-40 min. before the experiment. In some rats the injection of strophanthin was alternated with that of the same amounts (0.3 ml) of Ringer's solution.

Results. In 14 rats in series I, a background level was determined of sodium and aqueous solution consumed, and greater appetite was found for the sodium-glucose solution than for the aqueous glucose solution. Subsequent administration of strophanthin-K to ten rats, regardless of the dose, caused a perceptible increase in consumption of the aqueous solutions and a decrease in consumption of the sodium glucose solutions. Stoppage of the strophanthin injection resulted in rapid restoration of the original choice of solutions offered.

The four control rats registered as before, a greater appetite for the sodium than for the water solution. In two rats, administration of strophanthin was alternated with that of Ringer's solution. These animals displayed the above-described changes in appetite only on the days that strophanthin was administered (Figure 1).

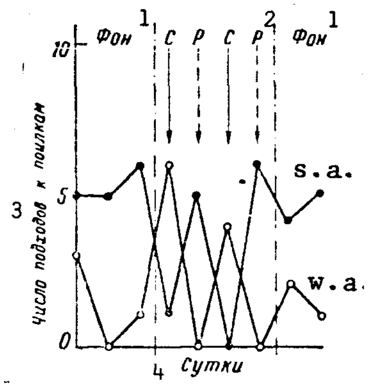

Figure 1

Effect of Administration of Strophanthin (S) and Ringer's Solution (R) on Sodium (s.a.) and Water (w.a.) Appetite.

(1) - Background; (2) - S R S R; (3) - Number of Approaches to Drinking Bowl; (4) - Days.

In evaluating these results, the question arose of whether the observed changes in appetite were associated with decreased consumption of sodium chloride and only with a relatively increased consumption of water, or whether in this case there was also a genuine increase in water appetite. It is known that rats require 40% glucose as an alimentary solution, and 8% as a potable solution (Refs. 1, 8). In four rats before administration of strophanthin a higher level of demand for the 40% glucose solution over 8% was noted. Administration of strophanthin caused increase in appetite for the 8% solution, while cessation of strophanthin restored the original choice. Therefore, a genuine increase in water appetite could be indicated.

Since the ratios of sodium and potassium in the cell and in the extracellular fluid are directly opposite, it seemed interesting to trace the effect of strophanthin on the potassium appetite. Seven rats were offered the choice between the 40% aqueous and potassium solutions of glucose. Before administration of strophanthin, all animals displayed a higher potassium appetite than for water. Strophanthin administration to four rats lowered their consumption of the aqueous and the potassium glucose solutions, but the potassium appetite remained high in relationship to total appetite, which also fell.

To give a more detailed characterization of the influence of strophanthin on potassium appetite, a supplementary series of experiments was conducted: ten rats registered a higher background level of consumption of the 8% aqueous solution of glucose than of the 8% potassium solution. Injection of strophanthin into six rats caused a noticeable increase in consumption of the potassium glucose solution in all of them, while cessation of the injection resulted in rapid restoration of the original choice. The control animals consumed the /1213 aqueous glucose solution in large quantities.

Table I gives the results of the experiments.

All data presented are statistically reliable.

Thus, when summing up the data on the effect of strophanthin on the state of specialized appetites in rats, we must note that strophanthin inhibits sodium appetite and stimulates potassium and water appetites.

Thus, the redistribution of water and ions between the extra- and intracellular fluids without any essential change in their content in the organism during inhibition of the sodium pump is capable of causing considerable displacements in the reactions of alimentary choice. In strophanthin administration,

TABLE 5

Working Solution	Pair of solutions being compared	Quantity of solution drunk (M ± m), ml		
		Before strophantin administration	During strophantin administration	After strophanthin administration
40% glucose solution	Aqueous	0.4 ± 0.03	2.6 ± 0.2	0.6 ± 0.03
	Sodium	4.35 ± 0.07	0.9 ± 0.1	3.3 ± 0.4
Aqueous solution of glucose	8%	0.35 ± 0.05	1.2 ± 0.3	0.4 ± 0.15
	40%	1.5 ± 1.0	0.5 ± 0.1	2.1 ± 0.6
40% glucose solution	Aqueous	4.2 ± 0.5	0.3 ± 0.08	4.0 ± 0.4
	Potassium	0.6 ± 0.1	3.8 ± 0.2	0.5 ± 0.1

they are: (1) increased water appetite, (2) decreased glucose consumption, (3) decreased sodium consumption, and (4) increased potassium consumption.

Bearing in mind that, in inhibition of the sodium pump, it is sodium which enters the cells, while potassium is transferred into the extracellular fluid, we must conclude that the above-mentioned shifts in salt appetite provide intracellular homeostatis, rather than extracellular. If the appetite chiefly regulated the extracellular concentration of potassium and sodium, then an increase in sodium and decrease in potassium appetite should be expected. In actuality, the opposite takes place. Together with this the increase in volume of intracellular and the decreased volume of extracellular fluid - an indirect indication of which is the increase in erythrocyte count from 7 to 9-12 million per cubic mm after strophanthin is administered - indicates that a decrease in the amount of extracellular fluid plays an important role in the rise of thirst.

The data on the substantial effect of the sodium pump on absorption of different substances takes us far from the usual views on the regulation of water and salt appetites. Indeed, the change in the latter is apparently associated not only with the elevation or reduction of the content of various substances in the organism, but also with the functional state of the mechanisms controlling their distribution between extra- and intracellular fluids. The action of the neural and hormonal factors on the appetite from this viewpoint also contains mechanisms determining the transfer of substances through cellular membranes. If the hypothesis is correct, then aldosterone stimulating the sodium pump should inhibit the potassium appetites, and elevate the sodium appetite. The same hypothesis admits that there are changes in appetite which do not ensure normalization of the basic blood constants. Thus, when the concentration of blood sodium falls, the consumption of sodium chloride usually increases, but, as has been shown in this paper, hyponatremia caused by strophanthin is accompanied by inhibition of sodium chloride consumption. It is important that in all cases the change in appetite favors the restoration of intracellular homeostasis.

The effect of strophanthin-K on the appetite is interesting in still /1214 another respect: under ordinary conditions - for example, when salts are artificially administered to the organism - the basic constants of the extra- and intracellular fluid change in a single direction (concentration of sodium or of potassium). The administration of strophanthin successfully produces shifts in different directions in the extra- and intracellular fluid, and therefore it is possible to evaluate the relative role of each of them in regulating the choice of salt.

I. P. Pavlov
Institute of Physiology
U.S.S.R. Academy of Sciences

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